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Defining partial response in inflammatory bowel disease: a Delphi consensus and economic evaluation

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Abstract

Background: Therapeutic goals in inflammatory bowel disease (IBD) are constantly evolving due to novel medical options and diagnostic tools, yet unmet clinical needs persist.

Objectives: We aimed to establish a consensus definition for partial responders in clinical practice, considered as patients failing to meet defined objectives within the desired time frame.

Design: A two-round Delphi consultation was held with IBD-specialized gastroenterologists.

Methods: The 22-item questionnaire covered four clinical scenarios: (1) moderate ulcerative colitis (UC); (2) acute severe UC; (3) luminal Crohn's disease (CD); and (4) perianal CD. Consensus was defined when ⩾70% of panellists agreed with a statement, rated using a 7-point Likert scale. We also analysed the associated annual costs for partial responders and patients in remission according to the agreed long-term definitions, based on a literature review and the experience of the scientific committee. Medication costs were excluded from the analysis.

Results: Sixty Spanish gastroenterologists with extensive experience in IBD management participated in the consultation. Consensus was achieved on partial response definitions with different criteria over time, including clinical scores, biomarkers and imaging or endoscopic examinations. The annual cost for partial responders and patients in remission was estimated at €2570.40 and €820.20 for UC, €1607.30 and €718.0 for luminal CD and €2886.70 and €888.80 for perianal CD, respectively.

Conclusion: The concept of partial responders has been defined in four clinical scenarios. Patients achieving prolonged remission could provide 55%–70% savings in non-pharmacological resource use and associated costs. Our study could help healthcare professionals in decision-making, ultimately improving patient care.

Plain language summary

Delphi questionnaire and cost analysis in inflammatory bowel disease

Treatment goals for inflammatory bowel diseases (IBD), like ulcerative colitis and Crohn's disease, are changing because of new treatments and better ways to diagnose these conditions. However, there are still some unmet needs in patient care.

The goal of this study was to define the term "partial responders," which refers to patients who don't fully meet treatment goals within the expected time.

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To do this, 60 doctors who specialize in IBD in Spain participated in a survey. The survey included 22 questions about four situations: moderate ulcerative colitis, severe ulcerative colitis, Crohn's disease in the intestines, and Crohn's disease around the anus. The doctors agreed on what it means to be a "partial responder" when at least 70% of them gave the same answer. The study also looked at the yearly costs for patients in remission and partial responders, based on existing research and expert opinions.

The results showed that doctors agreed on how to define partial responders using things like clinical scores, blood tests, and imaging exams. The study estimated the yearly costs for partial responders and patients in remission. For ulcerative colitis, it was €2,570.40 for partial responders and €820.20 for those in remission. For Crohn's disease in the intestines, it was €1,607.30 for partial responders and €718.0 for those in remission. For Crohn's disease around the anus, it was €2,886.70 for partial responders and €888.80 for those in remission.

The study concluded that the idea of "partial responders" was clearly defined in these four situations. It also showed that patients in long-term remission could save 55%–70% on non-medical costs. This research can help doctors make better decisions and improve patient care.

Keywords: healthcare costs, IBD, response to therapy

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Introduction

Inflammatory bowel disease (IBD) is characterized by heterogeneous clinical manifestations and a chronic relapsing-remitting course caused by the interaction of multiple factors such as genetics, gut microbiome dysbiosis and immune dysregulation.[1,2] The two main entities of IBD are ulcerative colitis (UC), affecting the colon and rectum exclusively, with continuous mucosal inflammation,[3] and Crohn's disease (CD), affecting any segment of the digestive tract and characterized by segmental and transmural involvement.[4] Symptoms of IBD mainly include rectal bleeding, abdominal pain, diarrhoea, defecatory urgency, perianal lesions and extraintestinal manifestations.[5] These symptoms, along with the associated comorbidities, significantly impact patient health-related quality of life (HRQoL) across physical, emotional, social and sexual domains,[6–8] and include limitations in regular physical activity, which may be further exacerbated by social and familial stigma.[9]

The onset of IBD typically occurs in young adults aged between 15 and 40 years, with a second smaller peak in incidence for people aged over 65.[10] In Spain, the estimated incidence of IBD in adults is 16.2 per 100,000 inhabitants, 7.4 for CD and 8.1 for UC.[11,12]

Therapeutic goals in IBD are evolving with the advent of novel treatment options (including biological therapies and small molecules) and diagnostic tools,[13] and focus on achieving and maintaining disease control, minimizing complications and sustaining prolonged periods of remission.[14] Assessing disease activity and therapeutic effectiveness requires outcomes reported by both healthcare professionals and patients.[15] Clinical response is defined as an improvement in symptoms and/or disease markers, but does not necessarily mean that the patient has achieved remission, which refers to the absence of signs and symptoms of active inflammation.[16,17] Over time, these concepts have evolved into the more comprehensive framework of 'disease clearance', which encompasses not only clinical remission but also biochemical, endoscopic and histological healing.[13,14,18,19] This composite outcome is increasingly recognized in clinical trials as a more rigorous and holistic measure of therapeutic efficacy.

These different remission domains are assessed using various scoring systems, including the Mayo score, the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) and the Crohn's Disease Activity Index (CDAI). However, there is some degree of heterogeneity among these measures, particularly regarding the definition and evaluation of mucosal healing.[18,20–22]

Despite substantial evidence demonstrating the value of these components, these broader definitions may not always be systematically applied in clinical practice and significantly hinder valid comparisons across trials.[22–24] This issue is particularly important in patients who do not achieve complete remission due to suboptimal treatment, failing to meet defined objectives within the desired time frame.[16,25–27] Thus, early identification of partial responders in routine clinical practice is crucial for timely diagnosis, intervention, better prognostic outcomes and optimization of HRQoL.[28,29] Furthermore, as in other chronic diseases, uncontrolled IBD may result in higher resource utilization and associated costs than controlled disease.[30–32] This highlights the importance of comprehensive remission as the primary therapeutic goal, both to improve patient outcomes and to reduce the overall burden of the disease.

For these reasons, this study aimed to reach a consensus on the concept of partial response to therapy for different clinical scenarios, and to analyse the direct costs associated with patients in remission and partial responders, considering the degree of disease control in the long term.

Materials and methods

The study was led by a multidisciplinary scientific committee with extensive experience in the management of IBD, and included four gastroenterologists and two hospital pharmacists. It was divided into four phases: (1) literature review; (2) discussion group; (3) Delphi consultation and (4) resource use estimation and associated cost analysis. The methodological protocol developed for the Delphi consensus is shown in Figure 1.

Literature review

A literature search was conducted in the Medline/PubMed database to identify current evidence on therapeutic goals in pharmacological treatment, including activity indices and time frames. The terms and search strategy are detailed in Supplemental Information (Table S1). Observational studies, phase III and IV clinical trials, systematic reviews, consensus documents and management guidelines published in English or Spanish from 2018 to 2023 were reviewed. For clinical trials involving biological treatments, the inclusion period was limited to 2 years, as this time frame ensures a focus on the most recent evidence and takes into account the rapid evolution of therapeutic strategies in this area. A manual search in grey literature sources was also carried out (Google Scholar).

Scientific committee

A discussion panel formed by six health professionals (gastroenterology ($n=4$) and hospital pharmacy ($n=2$)) was created to review the information identified in the literature search, define the clinical scenarios of interest and design the aspects to be explored in the Delphi consultation. Thus, all questionnaire items were developed based on the literature review and refined by the discussion panel to ensure neutrality and avoid leading statements. Due to the clinical heterogeneity of IBD, four clinical scenarios were defined: moderate UC (outpatient treatment); acute severe UC (hospital admission); luminal CD and perianal CD.

Delphi consultation

A national two-round Delphi consultation was conducted following the recommended Conducting and REporting of DElphi Studies (CREDES) guidelines.[33,34] This method was selected due to its ability to address unknown areas of a current key topic to achieve consensus. The first questionnaire included sociodemographic (three items) and professional experience variables (three items), followed by 22 Delphi statements related to the partial response concept in the short, medium and long term, grouped into the four previously defined clinical scenarios. In the first round, the statements derived from the comprehensive literature review and the discussion group were presented. Panellists rated their agreement with each statement using a predefined 7-point Likert scale (1 = strongly disagree, 4 = neither agree nor disagree, 7 = strongly agree). The statements that did not reach the predetermined threshold for consensus (⩾70% agreement) were

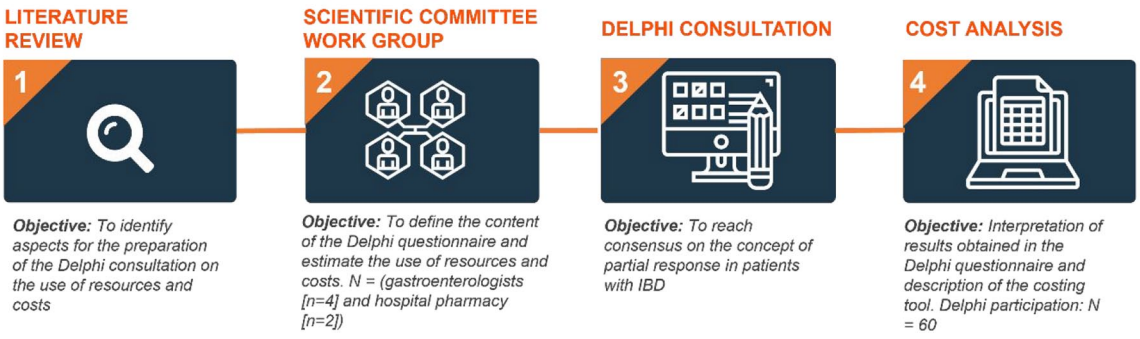

Figure 1. Flowchart of the methodological protocol for the Delphi consensus.

identified for further evaluation. The second-round questionnaire included only the statements for which consensus was not reached in the first round, with no modifications, enabling panellists to reassess their responses. Each Delphi panellist received their individual score for the first round and the overall agreement, allowing them to either confirm their response or change their opinion.

Potential panellists were identified by the scientific committee from among gastroenterologists with a particular interest in IBD and invited to participate via email. Each panellist received a link to the study questionnaire, along with a personalized username and password to log in, ensuring the anonymity of their answers. None of the participants had access to other members' answers.

The percentages described in the text refer to the final scores (score of the round in which consensus was achieved for each question, either first or second).

Resource use estimation and associated cost analysis

Based on the results of the literature review and the experience of the scientific committee, the resource use associated with patients in remission and partial responders (determined according to the agreed long-term definitions) was estimated. The analysis utilized a 1-year time horizon to capture long-term resource utilization. The list of identified resources included different types of medical visits (specialized and primary care, both in-person and virtual visits), common procedures for IBD patients (blood tests, stool analysis, colonoscopy and imaging procedures), as well as other resources such as emergency department visits, hospital admissions and surgical evaluations under anaesthesia. Unit costs for the analysis were obtained from official Spanish healthcare databases.[35] When different rates were observed for the same item across different regions of Spain, the mean cost was calculated. Detailed unit costs used for the calculations are provided in Supplemental Information (Table S2).

Statistical considerations

To assess the variability in frequencies or unit costs, values were adjusted between the specified minimum and maximum frequencies, with the mean value used as a baseline.

Ethical statement

No ethical approval was necessary for this study as it did not involve patients and no clinical records were accessed; only the panellists' perceptions were explored. The data obtained from the panellists' responses were anonymized and informed consent was obtained prior to the start of the study. Confidentiality of personal data was protected in accordance with applicable Spanish law.[36]

Results

Of the 70 gastroenterologists invited to participate in the Delphi consultation, 60 completed the first round (response rate: 85.7%), and 58 completed the second (response rate relative to the first round: 96.7%). The panellists had a mean experience of 20.4 years (standard deviation (SD) = 8.8) and most of them (90.0%) primarily practiced in specialized care centres (Table 1).

Table 1. Sociodemographic and professional experience characteristics.

Characteristics	Value
Sex, % (*n*)	
Male	33.3 (20)
Female	66.7 (40)
Age, years, mean (SD)	48.3 (8.6)
Professional experience, years, mean (SD)	20.4 (8.8)
Type of centre in which main professional activity is carried out, % (*n*)	
Primary care	1.7 (1)
Secondary care (specialized care in a regional hospital)	8.3 (5)
Tertiary care (specialized care in a referral hospital)	90.0 (54)
Number of IBD patients managed monthly, mean (SD)	167.9 (106.7)

IBD, inflammatory bowel disease; SD, standard deviation.

The study targeted professionals practicing in Spain, with representation from most Spanish regions.

A total of 22 statements were presented and consensus was reached on all of them (18 out of 22 in the first round and the remaining 4 in the second round). Ten statements were evaluated for UC, comprising eight for moderate UC (one for short-term, three for medium term and four for long term) and two for acute severe UC. In addition, 12 statements were evaluated for CD, comprising 8 luminal CD statements (1 short term, 3 medium term and 4 long term) and 4 perianal CD statements (1 short term and 3 long term; Table 2).

In moderate UC (outpatient treatment), the consensus definition for partial response includes different criteria over time. In the short term, it was defined as clinical improvement without achieving clinical response, established as a $\geqslant$50% decrease in two-item patient-reported outcome (PRO2; abdominal pain and stool frequency). In the medium term, it was described as improvement without achieving clinical remission – defined by PRO2 (rectal bleeding = 0 and stool frequency = 0) or Partial Mayo Scoring Index (total score $<$3 and subscores $\leqslant$1) – or achieving clinical remission with persistently elevated biomarkers (considering the normalization of faecal calprotectin to 100–250 μg/g). In the long term, it was defined as improvement without achieving clinical remission or achieving clinical remission with persistent inflammatory activity in biochemical parameters, imaging procedures or endoscopic examinations.

In acute severe UC (with hospital admission), the consensus for partial response was only defined in the short term, since over the medium and long term, this acute severe clinical profile converges to resemble that of the moderate form. In this case, the partial response refers to clinical improvement without achieving a clinical response within 3 days, or failing to achieve clinical remission after 30 days.

In luminal CD, the definition for partial response includes different criteria over time. In the short term, it was described as clinical improvement without achieving a clinical response, defined as a $\geqslant$50% decrease in PRO2 (abdominal pain and stool frequency). In the medium term, it was described as clinical improvement without achieving clinical remission, defined as PRO2 (abdominal pain $\leqslant$1 and stool frequency $\leqslant$3 or Harvey-Bradshaw Index (HBI) $<$5), or achieving clinical remission with persistent inflammatory activity in biochemical tests (considering the normalization of C-reactive protein to values under the lower limit of normal and faecal calprotectin to 100–250 μg/g). In the long term, it

Table 2. Delphi consultation results.

Clinical scenario	Statement	Agreement, %	Disagreement, %
Moderate UC (outpatient treatment)	*Short-term* partial response is considered when the patient		
	. . . presents clinical improvement without achieving clinical response[a]	91.7	–
	Medium-term partial response is considered when the patient		
	. . . presents clinical improvement without achieving clinical remission[b]	91.7	–
	. . . presents clinical remission[b] with persistently elevated biomarkers[c] (e.g. faecal calprotectin)	81.7	–
	. . . presents clinical remission,[b] normalized biomarkers[c] (e.g. faecal calprotectin), but requires corticosteroid use	–	94.8*
	Long-term partial response is considered when the patient		
	. . . presents clinical improvement without achieving clinical remission[b]	85.0	–
	. . . presents clinical remission[b] with persistently elevated biomarkers[c] (e.g. faecal calprotectin)	88.3	–
	. . . presents clinical remission,[b] normalized biomarkers[c] (e.g. faecal calprotectin), with persistent inflammatory activity in imaging procedures or endoscopic examinations	83.3	–
	. . . presents clinical remission,[b] normalized biomarkers[c] (e.g. faecal calprotectin), no inflammatory activity in imaging procedures or endoscopic examinations, but requires corticosteroid use	–	94.8*
Acute severe UC (admission)	*Short-term*[$] partial response is considered when the patient		
	. . . presents clinical improvement after 3 days without achieving clinical response[a]	88.3	–
	. . . presents clinical response after 30 days without achieving clinical remission[b]	70.7*	–
Luminal CD	*Short-term* partial response is considered when the patient		
	. . . presents clinical improvement without achieving clinical response[a]	91.7	–
	Medium-term partial response is considered when the patient		
	. . . presents clinical response without achieving clinical remission[d]	93.3	–
	. . . presents clinical remission[d] with persistently elevated biomarkers[e] (e.g. faecal calprotectin or C-reactive protein)	81.7	–
	. . . presents clinical remission,[d] normalized biomarkers[e] (e.g. faecal calprotectin or C-reactive protein), but requires corticosteroid use	–	87.9*

(Continued)

Table 2. (Continued)

Clinical scenario	Statement	Agreement, %	Disagreement, %
	Long-term partial response is considered when the patient		
	. . . presents clinical improvement without achieving clinical remission[d]	85.0	–
	. . . presents clinical remission[d] with persistently elevated biomarkers[e] (e.g. faecal calprotectin or C-reactive protein)	88.3	–
	. . . presents clinical remission,[d] normalized biomarkers[e] (e.g. faecal calprotectin or C-reactive protein), with persistent inflammatory activity in imaging procedures or endoscopic examinations	86.7	–
	. . . presents clinical remission,[d] normalized biomarkers[e] (e.g. faecal calprotectin), no inflammatory activity in imaging procedures or endoscopic examinations, but requires corticosteroid use	–	75.0
Perianal CD	*Short/medium*-term partial response is considered when the patient		
	. . . presents clinical improvement in the perianal area without achieving clinical response[f]	86.7	–
	Long-term partial response is considered when the patient		
	. . . presents clinical response[f] of the perianal disease, with persistent drainage of external openings (spontaneous or pressure)	76.7	–
	. . . presents clinical response[f] of the perianal disease, with one new external abscess or fistula opening in the past month	–	81.7
	. . . presents clinical response[f] of the perianal disease, with persistent inflammatory activity in imaging procedures	71.7	–

[a]Clinical response defined as a decrease of at least 50% in PRO2 (abdominal pain and stool frequency).
[b]Clinical remission defined as PRO2 (rectal bleeding = 0 and stool frequency = 0) or partial Mayo (<3 and no score >1).
[c]Normalization of faecal calprotectin to 100–250 µg/g.
[d]Clinical remission defined as PRO2 (abdominal pain ⩽1 and stool frequency ⩽3) or HBI < 5.
[e]Normalization of C-reactive protein (to values under the limit of normal) and faecal calprotectin to 100–250 µg/g.
[f]Clinical response defined as the closure of at least one external opening and absence of fistula drainage.
*Consensus reached in second round.
$Only the short-term concept was evaluated for this patient profile, since medium- and long-term would be considered equal to the moderate UC scenario.
CD, Crohn's disease; HBI, Harvey-Bradshaw Index; PRO2, two-item patient-reported outcome; UC, ulcerative colitis.

was defined as clinical improvement without achieving clinical remission or as clinical remission with persistent inflammatory activity in biochemical parameters, imaging procedures or endoscopic examinations.

Finally, in perianal CD, partial response was defined in the short-medium term as clinical improvement in the perianal area without clinical response, described as the closure of at least one external fistula opening and absence of fistula drainage. In the long term, clinical response in perianal disease was considered a partial response when there was persistent inflammatory activity in imaging procedures or drainage of external openings.

Resource use estimation and associated cost analysis

The annual frequency of resource use and associated cost analysis for each clinical scenario and level of improvement are detailed in Tables 3–5, and in Supplemental Information (Tables S3–S5).

It is important to highlight that this economic evaluation was only performed in three out of the four clinical scenarios defined (moderate UC, luminal CD and CD with perianal involvement), since the time frame set for the economic evaluation was 1 year. As agreed in the partial response definition and previously mentioned, the acute severe UC scenario converges to resemble that of the moderate UC scenario in the medium and long term.

The estimated annual cost for patients with moderate UC was €820.20 for those in remission, compared to €2570.40 for partial responders (Table 3). This results in an average annual cost difference of €1750.20 (Figure 2), primarily driven by a higher number of specialist visits and greater volume of procedures and tests.

The estimated annual cost for patients with luminal CD was €718.01 for those in remission, compared to €1607.35 for partial responders (Table 4). This resulted in an average annual cost difference of €889.33 (Figure 2), mainly derived from a higher number of specialist visits and greater volume of procedures and tests.

Finally, the estimated annual cost for patients with CD and perianal involvement was €888.82 for those in remission, compared to €2886.67 for partial responders (Table 5). This represents an average difference in annual costs of €1997.85 (Figure 2), mainly derived from the increased number of specialist visits, emergency department visits, hospital admissions, surgical evaluations under anaesthesia, procedures and tests.

Discussion

Several criteria are employed in the evaluation of disease activity in patients with IBD, including clinical, biological, endoscopic, histological and HRQoL parameters.[14,37–39] Each of these criteria offers valuable insights into specific domains of the disease, from symptomatic presentation and inflammatory markers to mucosal appearance and tissue pathology. However, it is relatively uncommon to adopt a comprehensive approach that integrates all these diverse criteria to assess disease activity holistically, particularly in clinical practice. Partial response is defined as an improvement in symptoms or disease markers within a particular time frame, but the patient may not necessarily achieve remission. Therefore, defining partial response is essential, as many patients can remain in a state of partial response for extended periods, resulting in the persistence of symptoms, reduced HRQoL, the possibility of experiencing complications and the need for closer follow-up.[40]

Currently, there are a limited number of publications that introduce the concept of partial response,[41–45] with only a few of them providing a heterogeneous definition thereof. For example, in UC patients, partial response has been described as a decrease of ≥ 2 in the partial Mayo score,[46–49] a decrease of >4 in the Ulcerative Colitis Disease Activity Index,[50] or a decrease of 5 in the Truelove-Witts Severity Index.[51] In CD patients, partial response has been described as a decrease in the CDAI of >70,[49,51] or as a score in the CDAI of between 180 and 220.[52] This lack of uniformity underscores the need for a consensus among experts in IBD management, especially as regards the scoring of partial response patients. Despite recent efforts to harmonize core outcomes in IBD trials, a standardized definition for partial response was not established.[53] In our study, PRO2 and HBI were used to determine luminal CD, while PRO2 and partial Mayo scoring assessed moderate UC. Although the use of different scores is commonly accepted in clinical practice, it would be beneficial to establish a consistent metric for measuring changes over time.

In this Delphi study, 60 gastroenterologists with extensive experience in IBD management agreed on the definitions for partial response in four different IBD clinical scenarios, aiming to guide healthcare professionals in optimizing their management in response to shifting treatment targets.

The Delphi statements were prepared considering the variables and therapeutic goals proposed by the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE-II) initiative, including the use of clinical indices such as PRO2, Mayo and HBI, the normalization of

Table 3. Costs associated with patients in remission and partial responders in moderate UC.

Resources	Moderate UC			
	Remission		Partial responder	
	Annual frequency	Cost, €, Mean [min, max]	Annual frequency	Cost, €, Mean [min, max]
Visits				
Gastroenterologist*	1.5	277.2 [239.7, 314.7]	5	786.7 [472.0, 1101.3]
In-person	1	239.7 [239.7]	2.5	599.2 [359.5, 838.8]
Virtual visit	0.5	37.5 [0, 75.0]	2.5	187.5 [112.5, 262.5]
Specialized nurse*	1.5	98.2 [78.53, 117.8]	5	294.5 [176.7, 412.3]
In-person	1	78.5 [78.5]	2.5	196.3 [117.8, 274.9]
Virtual visit	0.5	19.6 [0, 39.3]	2.5	98.2 [58.9, 137.4]
Endocrinologist	0	0.0	0	0.0
Primary care physician	0.5	31.7 [0, 63.4]	1.5	95.0 [63.4, 126.7]
Surgeon	0	0.0	0	0.0
Emergency department	0	0.0	0	0.0
Procedures				
Tests	4.5	196.8 [131.1, 262.3]	13.5	590.5 [524.6, 655.7]
Blood	1.5	17.8 [11.9, 23.8]	4.5	53.5 [47.5, 59.4]
Stool	1.5	56.8 [37.8, 75.71]	4.5	170.3 [151.4, 189.3]
Medication level	1.5	122.2 [81.4, 162.8]	4.5	366.7 [325.6, 407.0]
Colonoscopy**	1.0	216.3 [0, 432.6]	3.0	648.9 [432.6, 865.3]
Biopsy	0.5	204.9 [0, 409.8]	1.5	614.7 [409.8, 819.6]
Sample processing	0.5	11.4 [0, 22.85]	1.5	34.3 [22.8, 45.69]
MRI scan**	0	0.0	0	0.0
Ultrasound**	0	0.0	1.5	154.7 [103.2, 206.3]
Other				
Hospital admission***	0	0.0	0	0.0
Surgical evaluation	0	0.0	0	0.0
Total		820.2		2570.4

Annual frequency calculated as the mean frequency provided by the scientific committee.
*Fifty percent of the follow-up is carried out as a virtual visit.
**Not complementary procedures, therefore, one-third of the patients were assumed to have undergone each one.
***Two-day hospital admission was considered.
UC, ulcerative colitis.

biomarker levels (C-reactive protein and faecal calprotectin), and endoscopic healing (analysing the presence of inflammatory activity using imaging or endoscopic procedures).[14]

Other measures of remission associated with improved clinical outcomes described in the literature include sonographic healing[54] and histological healing.[55] However, due to the lack of

Table 4. Costs associated with patients in remission and partial responders in luminal CD.

Resources	Luminal CD			
	Remission		Partial responder	
	Annual frequency	Cost, €, Mean [min, max]	Annual frequency	Cost, €, Mean [min, max]
Visits				
Gastroenterologist*	1.5	236.0 [157.3, 314.7]	3.5	550.7 [472.0, 629.34]
In-person	0.75	179.8 [119.8, 179.7]	1.75	419.4 [359.5, 479.3]
Virtual visit	0.75	56.3 [37.5, 75.0]	1.75	131.3 [112.5, 150.0]
Specialized nurse*	1.5	88.4 [58.9, 117.8]	3.5	206.2 [176.7, 235.6]
In-person	0.75	58.9 [39.3, 78.5]	1.75	137.4 [117.8, 157.1]
Virtual visit	0.75	29.5 [19.6,39.3]	1.75	68.7 [58.9, 78.5]
Endocrinologist	0	0.0	0.63	96.2 [77.0, 115.5]
Primary care physician	0	0.0	1.5	95.0 [63.4, 126.7]
Surgeon	0	0.0	0	0.0
Emergency department	0	0.0	0	0.0
Procedures				
Tests	4.5	196.8 [131.1, 262.3]	9.0	393.7 [262.3, 524.6]
Blood	1.5	17.8 [11.9, 23.8]	3	35.7 [23.8, 47.5]
Stool	1.5	56.8 [37.9, 75.7]	3	113.6 [75.7, 151.4]
Medication level	1.5	122.2 [81.4, 162.8]	3	244.4 [162.8, 325.6]
Colonoscopy**	0.3	72.1 [0, 144.2]	0.3	72.1 [0, 144.2]
Biopsy	0.17	68.3 [0, 136.6]	0.17	68.3 [0, 136.6]
Sample processing	0.17	3.8 [0, 7.6]	0.17	3.8 [0, 7.6]
MRI scan**	0.17	73.1 [0, 146.3]	0.17	73.1 [0, 146.3]
Ultrasound**	0.50	51.6 [34.4, 68.8]	1.17	120.4 [103.2, 137.5]
Other				
Hospital admission***	0	0.0	0	0.0
Surgical evaluation	0	0.0	0	0.0
Total		718.0		1607.3

Annual frequency calculated as the mean frequency provided by the scientific committee.
*Fifty percent of the follow-up is carried out as a virtual visit.
**Not complementary procedures, therefore, one-third of the patients were assumed to have undergone each one.
***Two-day hospital admission was considered.
CD, Crohn's disease.

validated and reliable measuring tools, they remain secondary endpoints and not formal targets.[14] Moreover, it is not only the physical component that requires consideration, but also the psychological aspects related to IBD, as the disease has been reported to negatively impair

Table 5. Costs associated with patients in remission and partial responders in CD with perianal involvement.

Resources	CD with perianal involvement			
	Remission		Partial responder	
	Annual frequency	Cost, €, Mean [min, max]	Annual frequency	Cost, €, Mean [min, max]
Visits				
Gastroenterologist*	1.5	297.8 [198.5, 397.0]	3.5	694.8 [595.5, 794.0]
In-person	1.125	269.6 [179.8, 404.4]	2.625	629.1 [539.3, 719.0]
Virtual visit	0.375	28.1 [18.8, 37.5]	0.875	65.6 [56.3, 75.0]
Specialized nurse*	1.5	103.1 [68.7, 137.4]	3.5	240.5 [206.2, 274.9]
In-person	1.125	88.3 [58.9, 117.8]	2.625	206.1 [176.7, 235.6]
Virtual visit	0.375	14.7 [9.8, 19.6]	0.875	34.4 [29.5, 39.3]
Endocrinologist	0	0.0	0	0.0
Primary care physician	0	0.0	1.5	95.0 [63.4, 126.7]
Surgeon	0	0.0	2.5	366.1 [292.9, 439.3]
Emergency department	0	0.0	1.5	294.6 [196.4, 392.7]
Procedures				
Tests	4.5	196.8 [131.1, 262.3]	9.0	393.7 [262.3, 524.6]
Blood	1.5	17.8 [11.9, 23.8]	3	35.7 [23.8,47.6]
Stool	1.5	56.8 [37.9, 75.7]	3	113.6 [75.7, 151.4]
Medication level	1.5	122.2 [81.4, 162.8]	3	244.4 [162.8, 325.6]
Colonoscopy**	0.3	72.1 [0, 144.2]	0.3	72.1 [0, 144.2]
Biopsy	0.17	68.3 [0, 136.6]	0.17	68.3 [0, 136.6]
Sample processing	0.17	3.8 [0, 7.6]	0.17	3.8 [0, 7.6]
MRI scan**	0.17	73.1 [0, 146.3]	0.17	73.1 [0, 146.3]
Ultrasound**	0.50	51.6 [34.4, 68.8]	1.17	120.4 [103.2, 137.6]
Other				
Hospital admission***	0	0.0	0.15	253.4 [253.4]
Surgical evaluation	0.5	94.3 [0, 188.7]	1.50	283.0 [188.7, 377.3]
Total		888.8		2886.7

Annual frequency calculated as the mean frequency provided by the scientific committee.
*50% of the follow-up is carried out as a virtual visit.
**Not complementary procedures, therefore, one-third of the patients were assumed to have undergone each one.
***Two-day hospital admission was considered.
CD, Crohn's disease.

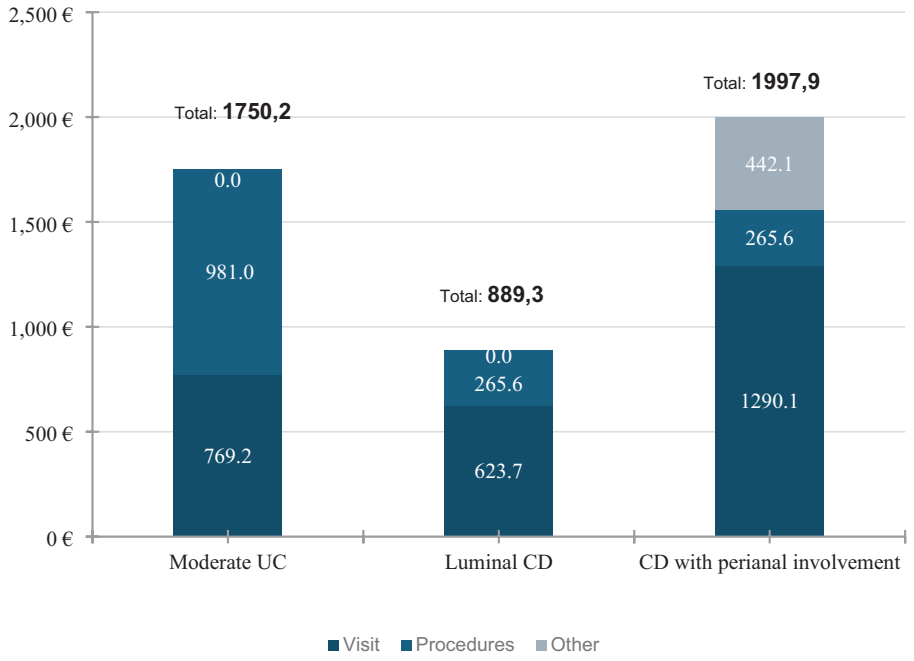

Figure 2. Difference in associated costs between patients in remission and partial responders.
CD, Crohn's disease; UC, ulcerative colitis.

HRQoL in the long term due to its chronic disabling nature.[56] In this context, many generic and disease-specific tools are available to measure the impact on HRQoL.[56] In addition, some patients in clinical remission may still experience symptoms or reduced quality of life (QoL) and could be considered partial responders over time. However, since the relationship between potential targets in IBD and HRQoL requires further study, the inclusion of HRQoL in the partial response definition was discarded by the scientific committee.

Regarding the definitions of partial response, in the cases of moderate UC and luminal CD, the panellists disagreed with the statement that the patient could be considered to have achieved medium- or long-term partial response if they required corticosteroid use. Corticosteroids are supported by substantial evidence as an effective first-line therapy for the treatment of active IBD flares. However, their use is associated with multiple adverse effects, and they tend to be ineffective when used as maintenance therapy. Therefore, they remain largely prescribed in the short term as initial management of active flares but are not adequate in long-term strategies.[57,58] This reflects emerging standards in clinical trials, where corticosteroid-free remission is assessed after several weeks off steroids. Although no consensus was reached, 12 weeks received the most support, and periods under 2 weeks were rejected as inadequate.[59] The definition of partial response in our study aligns with this premise regarding corticosteroid use, given their well-known higher risk of complications in the long term and their unsuitability as a maintenance therapy to sustain remission.[60,61]

The consensus achieved for the definition of partial response in acute severe UC, described as clinical improvement without achieving clinical response after 3 days or failing to achieve clinical remission after 30 days, was in line with the indications found in the literature regarding the need for initial medical management within this time frame, as this condition is considered a medical emergency. Otherwise, treatment failure would lead to rescue therapy and difficulty for these patients in achieving timely remission.[62]

Finally, in the case of perianal CD, the development of a new abscess or fistula did not meet the criteria for partial response in the long term, as it should be considered a clear sign of active disease.[63]

Standardizing the concept of partial response is of interest because patients who remain in such suboptimal therapeutic situations experience persistent symptoms, reduced HRQoL, the possibility of developing further complications and the need for closer follow-up.[26] Distinguishing between short- and long-term partial responses is essential for guiding clinical decision-making. A short-term partial response is characterized by clinical improvement without achieving a complete clinical response, while a long-term partial response reflects sustained treatment effects without achieving complete remission. These distinctions help in evaluating treatment efficacy and in identifying patients who may require adjustments to their therapy at an early stage. Furthermore, the consensus has defined four patient profiles, providing a practical framework for tailoring individualized treatment strategies.

It is equally important to establish practical clinical scenarios that prioritize optimal treatment goals, as delayed intervention can result in increased healthcare costs and worse patient outcomes.[64,65] For instance, patients in remission have been found to have significantly better QoL scores compared to those with active disease,[66,67] since they report less symptoms and higher satisfaction, mainly due to reduced disease activity and fewer relapses.[68,69]

Understanding the economic impact that patients in partial response have on the healthcare system in comparison to well-controlled patients in remission is also important. Achieving disease control among partial responders could present an opportunity for substantial economic savings by reducing the costs associated with uncontrolled disease.

A high economic burden is associated with IBD due to its early onset, chronic nature and growing prevalence worldwide.[70] Nevertheless, to our knowledge, this is the first economic evaluation of the costs associated with partial responders. Direct costs related to IBD patients have been described in the literature,[71–73] but in general and not accounting for differences in disease progression. The estimated annual costs in the present study ranged from €1604.70 up to €2886.70 for partial responders, while for patients in remission, this ranged from €718.01 to €888.82. This is in line with the average annual cost per patient, estimated at €2090 in 2006 in the Spanish setting, although this included pharmacological costs.[74] Our findings suggest a difference in annual costs of €889.33 and €1997.85 between patients in partial response compared to remission in luminal and perianal CD patients, respectively.

The deviation in associated costs for partial responders is mainly driven by the need for more medical visits, both specialized and primary care visits (in-person and virtual consultations), and the need for more tests and procedures during their follow-up. The difference may vary according to the clinician's criteria.

While our analysis suggests that partial responders may incur higher direct healthcare costs than those in remission, it does not imply equivalence to non-responders in terms of outcomes. Rather, it underscores the need for timely treatment optimization to prevent a sustained partial response from evolving into chronic, uncontrolled disease. It should also be considered that patients with 'silent' CD or IBD (asymptomatic patients who exhibit elevated subclinical inflammatory or key clinical parameters) have a higher risk of adverse outcomes, including disease progression and hospitalization, supporting the rationale for treatment intensification or the achievement of therapeutic targets even in the absence of overt symptoms.[75,76] Nonetheless, although achieving complete remission remains the primary therapeutic goal in IBD management, it is important to acknowledge that some patients may remain in a stable state of partial response that is pragmatically accepted by both physician and patient. In such cases, where symptoms are minimal despite persistent subclinical activity, further treatment escalation may not be warranted. As noted by Systrom et al., this situation may lead to healthcare costs that, although initially higher, tend to align over time with those of patients in remission. Recognizing this scenario reflects the complexity of real-world decision-making without diminishing the importance of striving for deep remission whenever possible.[77]

This study has several limitations and strengths. Regarding the limitations inherent to the technique, the consensus was based on the Spanish setting, and therefore, caution should be exercised when extrapolating results to other countries; in addition, a different consensus definition could have produced different results. Moreover, other professionals, such as surgeons or nurses,

and patient representatives, did not take part in the consensus. Although this may be considered a limitation, the exclusive participation of gastroenterologists was methodologically appropriate given their clinical expertise and primary responsibility in evaluating the therapeutic response in IBD. Furthermore, in the cost analysis of pharmacological treatment (including the need for treatment escalation), hospital visits for outpatient treatment, hospital pharmacy appointments and indirect costs were not considered, providing a partial economic view. Among the strengths, the incorporation of a multidisciplinary scientific committee, which provided diverse perspectives on IBD management, and the involvement of a substantial number of panellists with extensive experience in IBD management in the Delphi consultation, who ensured the representation of diverse clinical practices and experience, were pivotal.

Conclusion

A broad consensus was achieved on partial response definitions for four patient profiles in IBD. Our results suggest cost savings ranging from 55% to 70% in non-pharmacological resource use and associated costs when patients achieve prolonged remission. Further research is needed to determine whether short-term partial responders, if appropriately managed, can achieve better long-term outcomes than non-responders and whether both groups generate a similar economic burden. These findings raise the possibility that partial disease control may have an economic impact comparable to ineffective treatment, further emphasizing the need for optimized therapeutic strategies. Our study could help healthcare professionals in decision-making, ultimately improving patient care.

Declarations

Ethics approval and consent to participate

All the experts consented to participate in the expert panel. Johnson & Johnson and its employees were involved in the funding, concept design of the project, review and approval of the final publication, and are responsible for further enquiries; however, they have had no influence on the analysis and interpretation of results, which were performed by external experts.

Consent for publication

Not applicable.

Author contributions

Iago Rodríguez-Lago: Conceptualization; Data curation; Writing – review & editing.

Luis Menchén: Conceptualization; Data curation; Writing – review & editing.

José Germán Sánchez-Hernández: Conceptualization; Data curation; Writing – review & editing.

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Beatriz Garcillán: Conceptualization; Writing – review & editing.

Elia Moreno-Cubero: Conceptualization; Writing – review & editing.

Eugenia Vispo: Conceptualization; Writing – review & editing.

Eugeni Domènech: Conceptualization; Data curation; Writing – review & editing.

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Competing interests

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Availability of data and materials

Additional data are available from the corresponding author upon reasonable request.

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Supplemental material

Supplemental material for this article is available online.

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